



# **RETRO Rx: A new capability helping public health organizations**

March 29, 2019

## **New capability helps public health organizations predict, prepare, and respond to infectious disease outbreaks**

Measles. West Nile Virus. Hepatitis. Flu. Malaria. Tuberculosis. Zika.

The onset of any of these infectious diseases can cause great alarm if cases inexplicably begin appearing in very large numbers. During an infectious disease outbreak, as the case numbers increase, public health organizations look to their subject matter experts, analysts, and support staff for necessary assistance in deciding how to mitigate the immediate outbreak and possibly prevent disease re-emergence.

Analysts and support personnel face two challenges: a crippling lack of data and informational resources, especially in rural and developing countries, and a lack of processing and analysis capability to quickly interpret the data. Without data and analysis, developing a clear and effective intervention strategy is extremely challenging. There has been an absence of technology providing quick and accurate historical information and mitigation solutions until now.

A Los Alamos National Laboratory team of scientists and researchers has developed, deployed, and verified the Rapid, Easy Tools for Responding to Outbreaks and Re-emergence Events (RETRO Rx), a game changer in the area of disease forecasting and response. The suite of free, web-based tools together utilize historical data to provide rapid, easy-to-use, easy-to-interpret visual analytics that uses minimal data to provide meaningful and comprehensive results.

RETRO Rx is composed of two tools, Analytics for Investigation of Disease Outbreaks (AIDO) and Re-emerging Infectious Disease (RED) Alert. These tools fill a need by contextualizing disease outbreak data to provide situational awareness and actionable information.

LANL developers Ashlynn Daughton (A-1, Information Systems and Modeling) and Alina Deshpande (B-10, Biosecurity and Public Health) discuss RETRO Rx infectious disease re-emergence results

# Significance of the Work

The AIDO tool (<https://aido.bsvgateway.org/>) is used in the early stages of an outbreak. Its similarity algorithm compares data from an unfolding event to a library composed of 650 outbreaks across 39 diseases. Each comparison, ranked from most to least similar, has visual analytics and descriptive information so users can learn from past disease events, contributing factors, and mitigation strategies. Each outbreak has three types of analytics: outbreak comparison, anomaly detection and short-term forecast.

The analytics combined with the historical information becomes actionable information to help users decide how to best mitigate the outbreak. The response may include a vaccine campaign, quarantine, re-allocation of resources etc.

Here's how it works. Users enter the AIDO website and select the disease in question from a dropdown menu. Users enter required outbreak-specific information (country, case count, date of first reported case, and date of last reported case) and additional disease-specific factors if they are known (physician density per 1000 population, percentage of population vaccinated etc.). The AIDO similarity algorithm then takes the submitted information and compares the data to a library of representative historical outbreaks to complete a picture of the currently unfolding outbreak.

Because each disease has unique factors that influence the case count and duration of the outbreak, each has different information required that will provide various points of comparison used in the similarity algorithm. For example, the optional entry fields for measles are vaccination percentage of the country and region, climate, and physician density; whereas the optional entry fields for Q fever are reported contact with animal hosts, human development index, affected animals, and proximity to farm animals. The severity and duration of measles is heavily affected by access to vaccines and medical treatment, whereas Q fever's outbreak severity and duration is closely connected to exposure to infected animals.

After the user has entered the required outbreak-specific information and if known, disease-specific properties, the algorithm returns a list of similar outbreaks of the same disease. The disease-specific properties act as population-level signatures that help match a user's circumstances to historical outbreaks.

The RED Alert tool (<https://redalert.bsvgateway.org/>) is used after an outbreak has ended and addresses an additional need. Previously re-emergence had not been defined by experts with specific criteria, which led to irreproducible assessments of high-consequence, public-health events. This in turn may have led to poor disease response prioritization, misallocation of resources, and ineffective mitigation.

RED Alert uses a machine-learning approach to detect potential re-emergence. It employs a LANL-developed algorithm that computes disease incidence over the past several decades to determine if the present outbreak changes the current trend enough to be classified as potentially re-emergent or not, both locally and globally. RED Alert also informs users about factors that may contribute to re-emergence (e.g., low vaccination rates, occupational exposure, urbanization, inadequate sanitation etc.) and compares the local values from the outbreak location to global median values. Using historical and comparative information, RED Alert provides an early warning to decision-makers who can then implement protocols to protect populations from local and global public health crises.

# Achievements

RED Alert computes disease incidence and then re-emergence for a single disease across the entire world going back ten years from the input outbreak data. For a 2018 hypothetical measles outbreak illustrated below, the third graphic (C) would compute and display re-emergence events for measles from 2009 to 2018 across the world. Potential global re-emergence in this analysis can be detected as early as 2009. Of note, global re-emergence of measles was not described in the literature by experts until 2001/2012.

Is there a potential for global re-emergence? In 2009 (A), re-emergent measles outbreaks are found in Africa and Asia. In 2011 (B), the potential for measles re-emergence has come to both North and South America. In 2014 (C), it continues to spread east but does not appear again in the western continents. In 2018 (D), the inputted data (a hypothetical outbreak in Canada of 500 cases) appears.

Like AIDO, RED Alert is a free, web-based tool where users enter minimal outbreak data and receive useful disease-specific information and visual analytics to support their decision-making. However unlike AIDO, RED Alert is used after an outbreak has ended. It provides warning of potential re-emergence, locally and globally, and highlights factors that may contribute to re-emergence. This tool covers diseases recommended by experts at the World Health Organization including measles, dengue, yellow fever, and cholera.

After all necessary information is entered, RED Alert's algorithm classifies the input as potentially re-emergent or not and provides three tabs of analysis. The first tab provides visual responses to the following three questions:

1. Does this event represent a possible re-emergence of this disease?
2. What are potential contributing factors?
3. Is there is potential for global re-emergence?

Armed with this information decision makers can develop a comprehensive plan for effective prevention or containment of disease re-emergence both locally and globally.

The two complementary tools in RETRO Rx, AIDO and RED Alert, fill a need in the infectious disease surveillance community to examine massive amounts of historical data, compare it to present day situations, and to provide valuable information used for mitigation strategies. Unlike traditional models, these tools can be accessed and used by analysts, scientists, practitioners, decision-makers, and the general public. They are available via the Internet, are cost free, and have been evaluated by external entities such as Centers for Disease Control and Prevention and the National Bio-surveillance Integration Center. These evaluators found these tools easy to use and described them as research at fingertips and an excellent tool to train global epidemiologists.

RETRO Rx requires minimal effort and expertise from users and yet brings together a wealth of data to produce diverse visual analytics paired with detailed descriptions that are easily digestible. AIDO guides users at the early stages of an outbreak by comparing the current situation to historic outbreaks. RED Alert provides a broad historical picture of disease incidence to detect re-emergence at its earliest stages, both locally and globally, after an outbreak has ended. The RETRO Rx tools can be used for research, decision-making, analysis, and training and education. Foremost, RETRO

Rx compiles and presents data and analysis in a clear, concise visual format to support disease mitigation and prevention planning. This technology pushes the state of the art forward in disease forecasting and provides public health organizations with a powerful tool when time, resources, and action matter most in protecting the public's health.

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